

### **REMARKS/ARGUMENTS**

Applicants acknowledge receipt of the Office Communication dated March 9, 2004. In the Office Action dated March 9, 2004, (1) allowed claims 6 and 18-23, (2) rejected certain claims under 35 U.S.C. § 102(b), and rejected certain claims under 35 U.S.C. § 103(a). Applicants respectfully request consideration of the amendments and remarks, and withdrawal of the remaining rejections.

#### **Status of the Claims**

Claims 6 and 18-23 are allowed.

Claim 25 stands canceled.

Claims 1-5, 7-17, 24 and 26 are rejected.

Claims 1, 9 - 13 and 26 are currently amended.

New claims 27 - 29 have been added

Claims 1-24 and 26 - 29 are pending.

#### **Rejection of Claims Under 35 U.S.C. § 102(b)**

Claims 9-12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,393,739 (Bentz et al.). It is alleged that Bentz et al. teaches a combination of BMP and TGF- $\beta$  (col. 5, line 9), and that synthetic or recombinant forms would be free of histones and ribosomes (col. 5, lines 19-20). Applicants have amended claims 9 and 11 to make it clearer that the composition comprises a "bone protein mixture" which has been depleted of histones (claim 9) or ribosomes (claim 11) and in which at least one growth factor retains native post-translational modifications. As defined on page 5 of the specification, "bone protein" or BP refers to a certain bone protein mixture (see Figures 1, 4 and 15A-B, for example). The amendment is also supported in the specification at page 19, lines 2-3; 4-5; and 13-16, for example, where it is taught that the functional derivatives of some of the components of the bone protein (BP) mixture are in a glycosylated or phosphorylated form; and that "care must be taken in preparing BP not to degrade these functional modifications." By contrast, a combination of pure, synthetic or recombinant BMP with a TGF- $\beta$  protein, as allegedly taught by Bentz et al., while lacking histones and ribosomes, would not comprise the same bone protein mixture of any of claims 9-12.

Claim 26 is rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Patents 5563124, 5371191, and 5290763. It is said that the mixture of Figure 1 would inherently promote angiogenesis, regardless of whether that property was recognized at the time. Claim 26 is currently amended to

require that the wound is an area where osteogenesis is not desired. For example, a skin wound or a diabetic ulcer is an area where osteogenesis is implicitly not sought (see page 15, lines 7-20 of the specification, for example). Histological analysis of skin wound healing specimens was consistent with epithelialization (page 10, lines 17-25). By contrast, the methods disclosed in U.S. Patents 5563124, 5371191, and 5290763 do not teach applying the BP mixture to a site other than one where osteogenesis is desired and specifically sought.

#### **Rejection of Claims Under 35 U.S.C. § 103(a)**

Claims 1, 3-5, 7 and 8 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Wang et al. 2001 in view of Cerletti et al. The Office Action takes the position that recombinant proteins produced in mammalian cells are free of histones and ribosomal proteins and would inherently be in their native modified form.

Claims 13-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Wang et al. 2000 in view of Bentz et al. and further in view of Ksander et al. Claim 13 has been amended similarly to claim 1, and now requires a bone protein mixture depleted of histones or ribosomes, or depleted of both. Even if the pure or recombinant growth factors were combined in the suggested manner, the resulting mixture would not comprise the histone and/or ribosome depleted "bone protein" mixture as defined in Applicants' specification (e.g., page 5, lines 4-29; page 9, lines 24-25).

#### **Other amendments**

Claims 10 and 12 have been amended to improve claim form, without changing the scope, by rewording the term "mixture of proteins" as "bone protein mixture," in conformity with the bone protein mixture (BP) as defined in the specification.

For consistency, claims 9, 11 and 13 have been further amended to require that the composition is active for promoting skin wound healing without inducing osteogenesis when implanted at a site in need of skin wound healing. This amendment is supported in the specification at page 15, lines 7-20, for example. It is implicit that osteogenesis is not desired in skin wound healing or in healing a diabetic ulcer.

New claim 27, which depends from claim 11, has been added to ensure coverage of a specific embodiment to which Applicants are entitled. This claim is supported in original claims 1-3, for example. This claim distinguishes over the cited references for at least the same reason as claim 11.

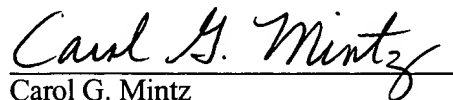
New claim 28 depends from claim 1 and recites certain tryptic peptide fragment characteristics of the bone protein mixture employed in claim 1. This amendment is supported in Figures 15A and 15B, and in the specification at page 16, lines 5-8 and 18-23, for example.

New claim 29 depends from claim 1 and is supported in the specification at page 15, lines 6-18, for example.

### **Conclusion**

Applicants may have at times referred to claim limitations in shorthand fashion, or may have focused on a particular claim element. This discussion should not be interpreted to mean that the other limitations can be ignored or dismissed. The claims must be viewed as a whole, and each limitation of the claims must be considered when determining the patentability of the claims. Moreover, it should be understood that there may be other arguments with respect to patentability which have yet to be raised, but which may be raised in the future. All of the pending claims are believed to be free of the prior art, and reconsideration and withdrawal of the rejections are respectfully requested. Should any fees have been inadvertently omitted, or if any additional fees are required or have been overpaid, please appropriately charge or credit those fees to Deposit Account Number 03-2769 of Conley Rose, P.C., Houston, Texas, and consider this a petition for any necessary extension of time.

Respectfully submitted,



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